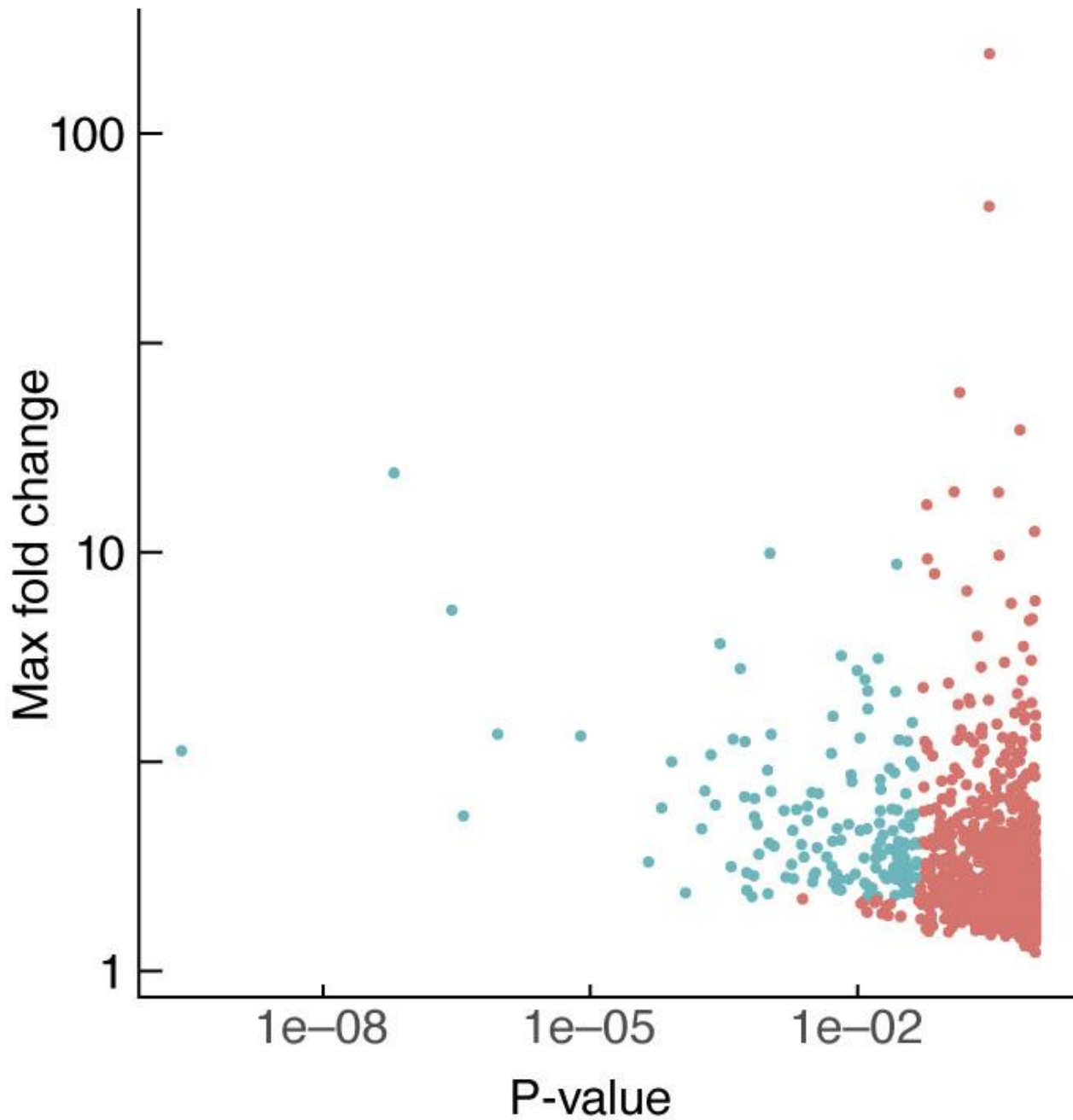


In the format provided by the authors and unedited.

Proteomic analysis of postsynaptic proteins in regions of the human neocortex

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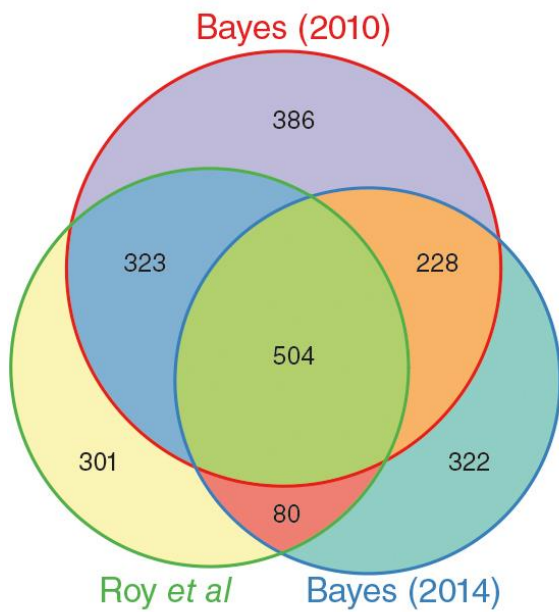
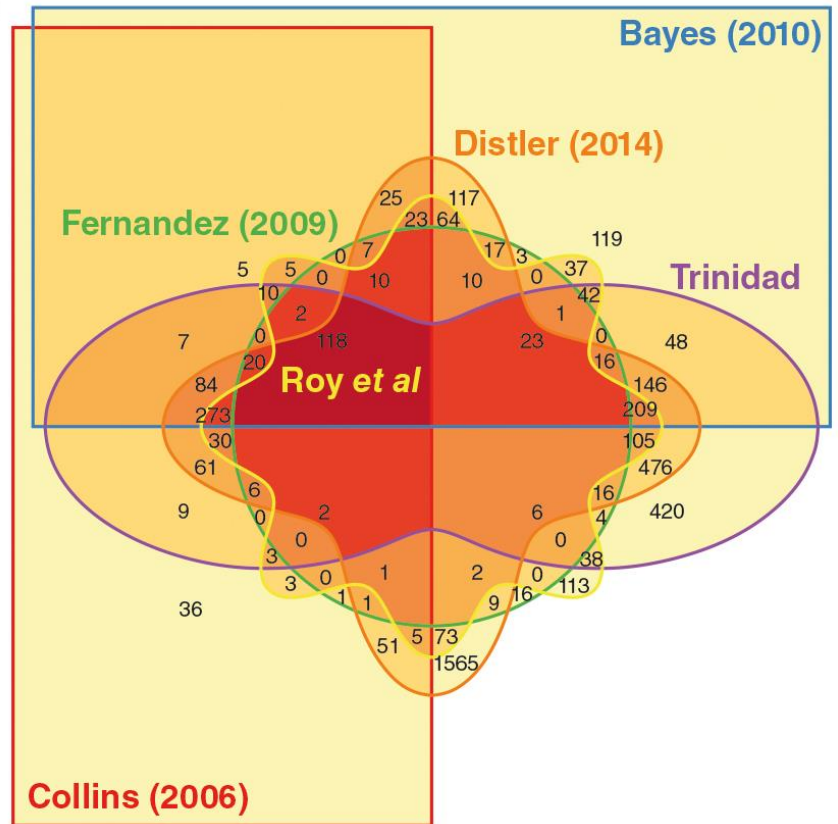
¹Genes to Cognition Program, Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK. ²School of Informatics, University of Edinburgh, Edinburgh, UK. ³Lilly Research Centre, Eli Lilly & Company, Erl Wood Manor, Windlesham, UK. Marcia Roy and Oksana Sorokina contributed equally to this work. *e-mail: seth.grant@ed.ac.uk



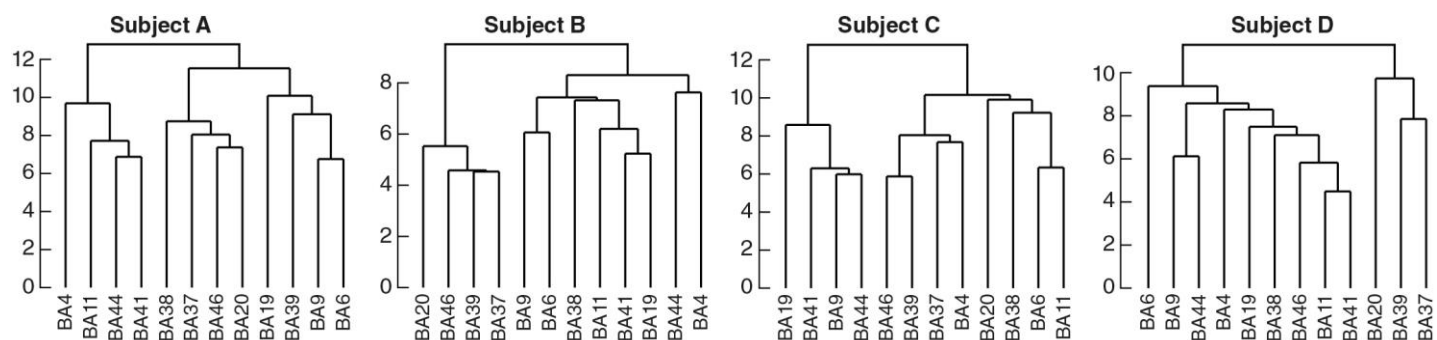
Supplementary Figure 1

Distribution of ANOVA P-values for differentially expressed genes

The magnitude of Anova P-value (x-axis) plotted against the maximum fold change (y-axis) for differentially expressed proteins. Dots correspond to specific proteins (total 1215). Green, 149 differentially expressed proteins with level of significance $p < 0.05$ and fold change > 1.5 .

a**b****Supplementary Figure 2****Overlap between the 1,213 PSD proteins identified in this study and other published synaptic proteomes.**

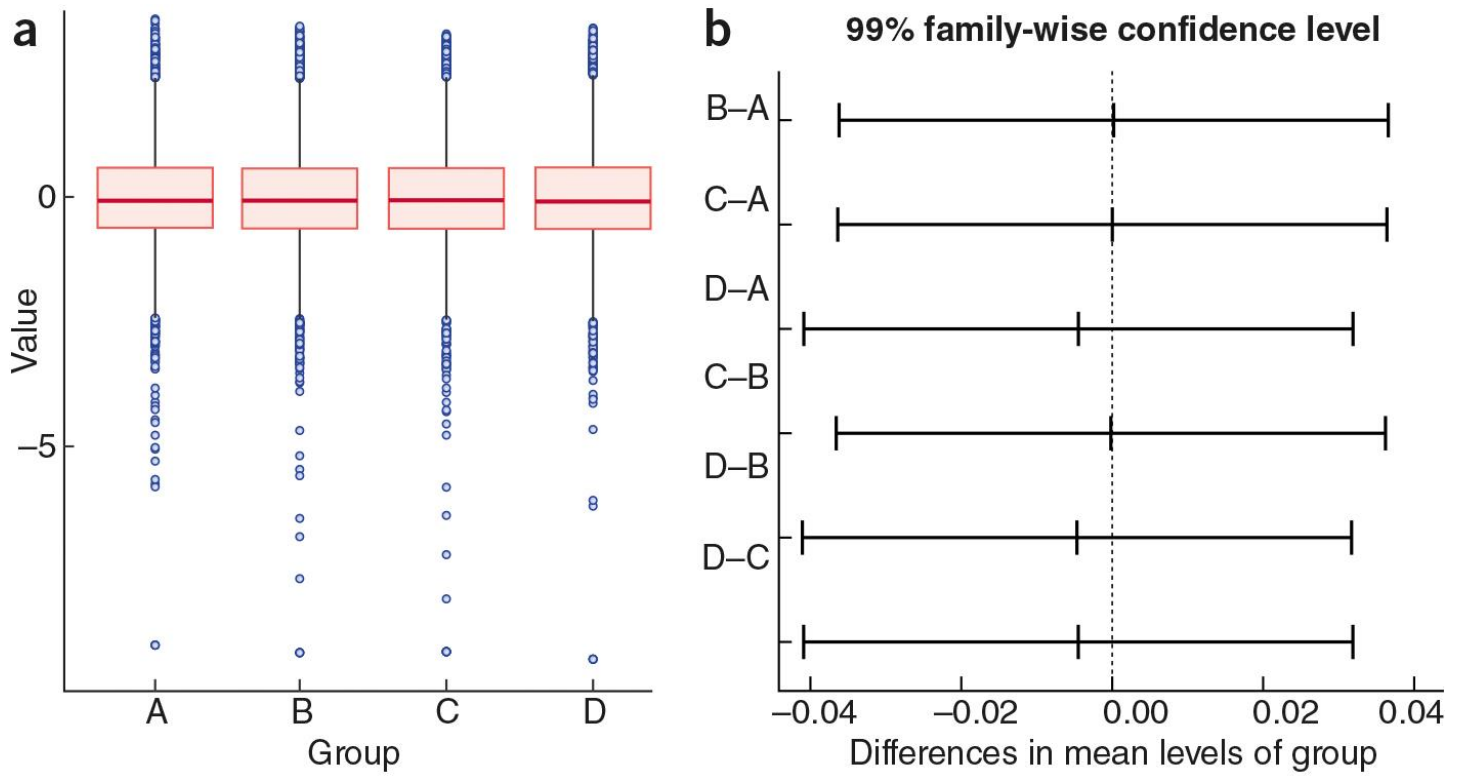
Overlap between the 1,213 PSD proteins identified in this study and other published synaptic proteomes. A) Venn diagram showing the overlap between this study and the human PSD proteomes published in Bayes *et al.*, 2011 and Bayes *et al.*, 2014. B) Venn diagram showing the overlap between this study and the PSD proteomes published in rat and mouse models from Distler *et al.*, 2014, Collins *et al.*, 2006, Fernandez *et al.*, 2009 and Trinidad *et al.*, 2008.



Supplementary Figure 3

Similarity of the PSD proteome between individuals.

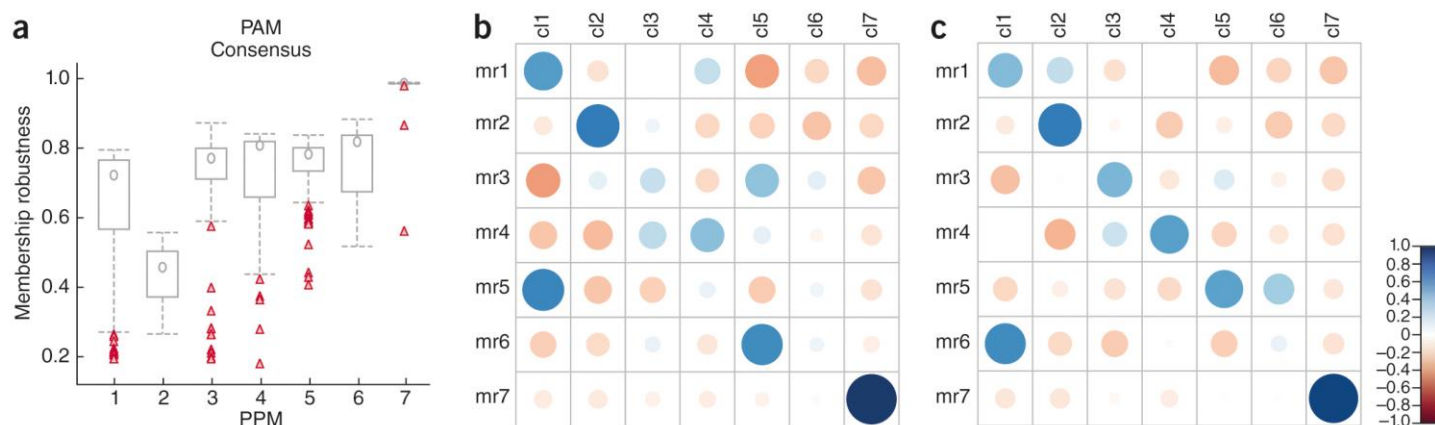
Similarity of the PSD proteome between individuals. Individual clustering dendrograms displaying the similarities between the 12 neocortical regions based upon PSD proteome abundances observed for each individual: A) SD025/13, B) SD042/13, C) SD032/13 and D) SD023/13.



Supplementary Figure 4

Results of the Tukey test.

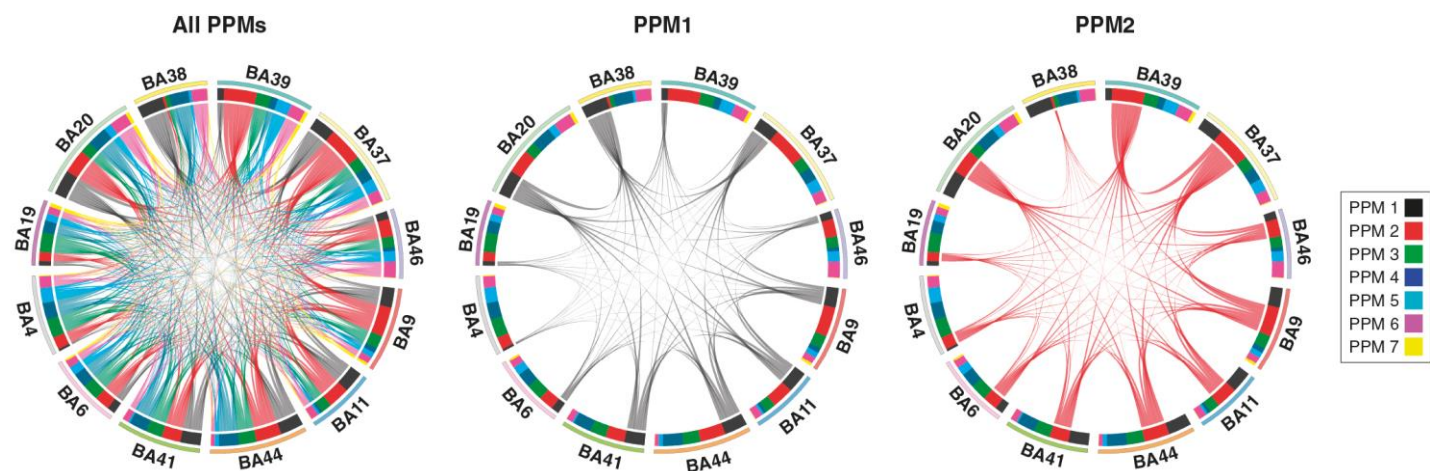
(A) Confidence intervals for the mean PSD protein abundance (Y-axis) plotted for each individual brain A) SD025/13, B) SD042/13, C) SD032/13 and D) SD023/13 (y-axis). (B) Pairwise comparison of the PSD proteome abundances in individuals A-D.



Supplementary Figure 5

Effect of individual variation on PPM robustness.

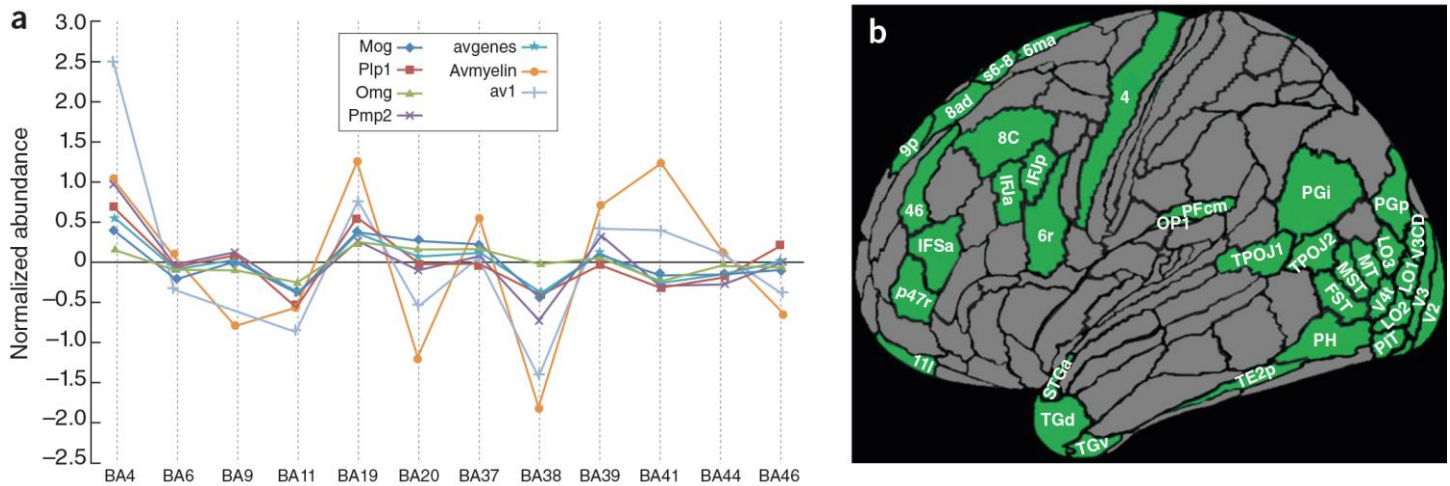
Effect of individual variation on PPM robustness. (A) Bootstrap analysis of PPM cluster robustness with k-means and PAM methods shows all modules were found to be stable (≥ 0.5 membership robustness). (B) Correlation of the PPMs/clusters across three combined samples (omitting the longest postmortem interval sample) (y-axis) and all four samples (x-axis). (C) Correlation of the PPMs/clusters between three combined samples (omitting the female sample) (y-axis) and all four samples (x-axis). Cr, cluster number; Mr, PPM number.



Supplementary Figure 6

Circos plots showing circular hierarchical clustering of the distribution of PPMs in 12 BAs

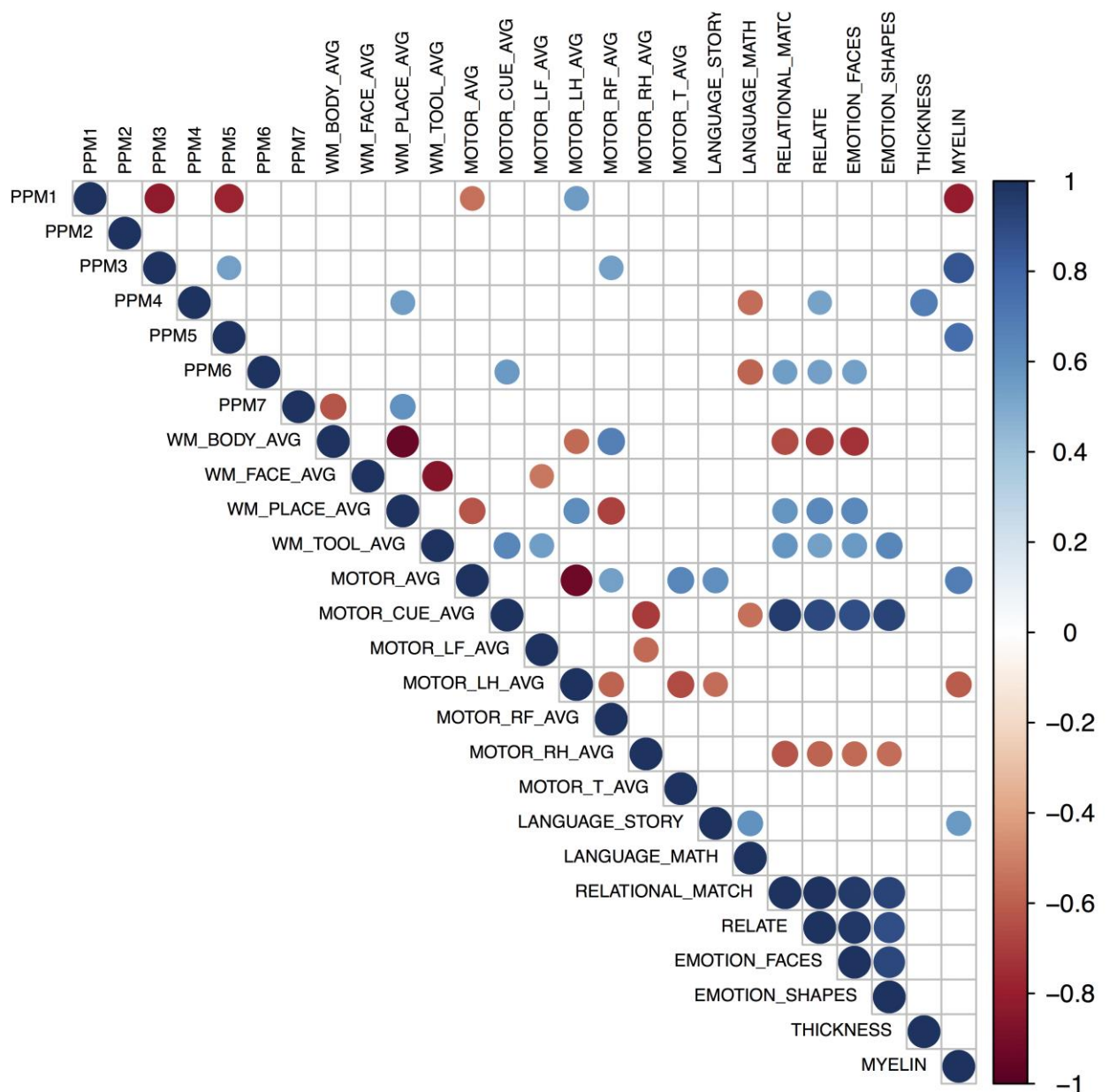
Circos plots showing circular hierarchical clustering of the distribution of PPMs in 12 BAs. Shown left, an overlay of all seven protein modules for all 12 cortical regions and individual plots of PPM1 (middle) and PPM2 (right) illustrate differential distributions. PPM 1 (black), PPM 2 (red), PPM 3 (green), PPM 4 (blue), PPM 5 (cyan) and PPM 6 (magenta) and PPM 7 (yellow). Width of the link is proportional to the fraction of the regional proteins contributed while its color corresponds to the respective PPM.



Supplementary Figure 7

Alignment of BAs in our study with the multimodal parcellated human cortex from the Human Connectome Project (HCP).

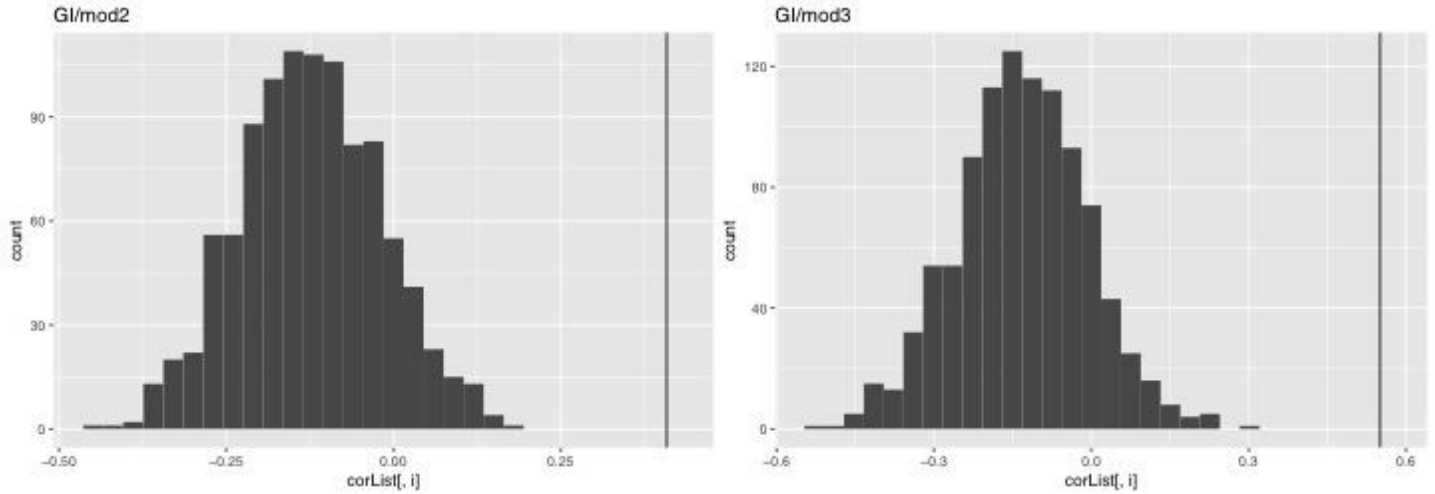
Alignment of Brodmann areas (BAs) in our study with the multi-modal parcellated human cortex from the Human Connectome Project (HCP). A) Line plot showing the trends in abundance for the four myelin proteins (Mog, dark blue; Plp2, red; Omg, green; Pmp2, purple), the average abundance of all four proteins (Avgenes, shown in cyan) and the average myelin abundance detected by MRI reported by Glasser *et al.*, 2016 from all parcels corresponding to BAs (Avmyelin, shown in orange) and from selected parcels, which give the best correlations score (av1, shown in light blue). B) Atlas of 40 HCP regions (annotated) corresponding to BA areas used for synapse proteomics.



Supplementary Figure 8

Correlations between the Postsynaptic Proteome Module (PPM) abundance and task-fMRI scores across 12 Brodmann areas.

Significant correlations between the Postsynaptic Proteome Module (PPM) abundance (averaged protein abundance for respective module) values and structural (Thickness, myelin) and task-fMRI scores across 12 Brodmann areas. The coefficients with an absolute value above 0.53 were significant at the FDR level 5%. Scale bar indicates positive and negative correlations. See Methods and supplementary Table 12 for definitions of fMRI nomenclature.



Supplementary Figure 9

Results of resampling test for PET

The distribution of correlation scores obtained for 10,000 reshuffled samples is shown for module2/GI and module3/GI pairs. Note that that the observed correlation values (vertical black line) lie far from the random distribution, indicating that the observed correlation with PET data is extremely unlikely to have occurred by chance (resampling-based q-value $< 10^{-4}$).